Clinica Chimica Acta 465 (2017) 34–39

Contents lists available at ScienceDirect

Clinica Chimica Acta

journal homepage: www.elsevier.com/locate/clinchim

Prevalence of thyroid dysfunction and autoimmunity in the older population and implications of age-specific reference ranges

Flora Veltri [a], Francisco Oliveira Rocha [b], Dominique Willems [c], Jean-Philippe Praet [b], Lidia Grabczan [a], Pierre Kleynen [a], Thierry Pepersack [b], Kris Poppe [a,*]

[a] Department of Internal Medicine, Université Libre de Bruxelles (ULB), Rue Haute 322, 1000 Brussels, Belgium
[b] Endocrine Unit, Department of Clinical Chemistry of the Centre Hosptilalier Universitaire Saint Pierre, Université Libre de Bruxelles (ULB), Rue Haute 322, 1000 Brussels, Belgium
[c] Geriatric Unit, Department of Clinical Chemistry of the Centre Hosptilalier Universitaire Saint Pierre, Université Libre de Bruxelles (ULB), Rue Haute 322, 1000 Brussels, Belgium

ARTICLE INFO

Article history:
Received 15 September 2016
Received in revised form 8 December 2016
Accepted 9 December 2016
Available online 15 December 2016

Keywords:
Age-specific TSH reference ranges
Older
Thyroid function and autoimmunity

ABSTRACT

Objective: To investigate the prevalence of thyroid dysfunction and autoimmunity (TAI) and to determine age-specific reference ranges in individuals <60 and ≥60-year-old. Furthermore we investigated the impact of the age-specific reference ranges on the prevalence of thyroid dysfunction.
Design: Retrospective analysis of laboratory data collected over six months in 2015, mainly from individuals consulting the outpatient clinic.
Method: Data from 676 individuals were withheld, after having applied strict exclusion criteria to avoid confounders. After exclusion of individuals with TAI (TPO-abs >60 kIU/L) and/or outliers, data of 547 individuals were used to determine age-specific reference ranges. The prevalence of subclinical hypothyroidism (SCH) and subclinical hyperthyroidism (sch) was determined according to the reference ranges from the commercial assay and also according to the calculated age-specific reference ranges. From our study population.
Results: From the 676 individuals included, 559 (83%) were <60 year-old and 117 (17%) ≥60 year-old. The prevalence of sch and TAI was comparable between both groups (8.6% vs. 13.7% and 15.4% vs. 20.5% respectively). The prevalence of SCH was significantly higher in individuals ≥60 years, compared to that in individuals <60 years (14.5% vs. 5.4%; $p < 0.001$). The calculated 2.5 and 97.5 percentile for the age-specific TSH range was 0.24 and 4.4 mIU/L in individuals <60 years and 0.15 and 8.2 mIU/L in individuals ≥60 years. When these the prevalence of sch and SCH was then determined on the basis of the age-specific reference ranges, the prevalence of SCH significantly decreased in individuals ≥60 years (14.5% to 5%; $p = 0.027$) and it then became comparable with that in individuals <60 years (5% vs. 3%).
Conclusions: The prevalence of SCH was higher in individuals ≥60 years, compared to that in individuals <60 years, but when age-specific TSH reference ranges were used, it was comparable between both study groups. In order to avoid misclassification in older individuals, it is important to use age-specific reference ranges in daily clinical practice

1. Introduction

Thyroid dysfunction is one of the most a common endocrine disorder in the general population and is often detected in a preclinical stage as subclinical hypo- or hyperthyroidism due to systematic screening programs, mainly applied in adults. Several studies have shown that the prevalence of both SCH and sch increased with age and f.i. in the Colorado study, the prevalence of SCH was ~2–10% in individuals <60 years and ~6–20% in those ≥60 years [13,46]. The increased prevalence of SCH in the older population might be has often been attributed to an increase in TAI, but in the NHANES III study, it was shown that serum TSH increased independently from that of TAI [24]. A number of changes in thyroid physiology may contribute to that increase, such as an increased hypothalamic/pituitary sensitivity to the negative feedback of the peripheral hormones (leading to decreased serum TRH/TSH secretion), and a decreased iodine uptake and deiodinase activity [7].

In the older population, the diagnosis of SCH is often challenging due to the presence of confounders, such as the non-thyroidal illness syndrome and the intake of medications that interfere with normal thyroid metabolism [26,27].

The increased prevalence of sch is probably due to an increased nodularity of the thyroid with the development of autonomous nodules, a feature that appears is more frequent in areas with (borderline) iodine deficiency [1].

* Corresponding author at: Department of Endocrinology, University Hospital CHU-St-Pierre, Université Libre de Bruxelles (ULB), Rue Haute 322, 1000 Brussels, Belgium.
E-mail address: kris_poppe@stpierre-bru.be (K. Poppe).

http://dx.doi.org/10.1016/j.cca.2016.12.008
0009-8981/

The importance of SCH and sch lies in their association with a number of cardiovascular co-morbidities, general complaints and neurocognitive disorders. In case of SCH, these co-morbidities are in case of SCH, an atherogenic lipid profile, heart failure, endothelial dysfunction, cerebro-vascular accidents and cognitive impairment [6,12,14,21]. Finally, sch and SCH are associated with an increased all-cause mortality rate [2,44]. In some of those studies, the association between SCH and the above mentioned co-morbidities remained absent in the older patients of the study group in contrast with that in the younger ones [2, 14,16,37,39]. In "very old" people (>85 years), SCH has even been associated with longevity [18,22], in part due to genetic polymorphisms in the TSH receptor, but others pathways might also have contributed to this association [4,10].

Several studies have shown a positive impact of LT4 treatment on a number of outcomes, such as fatigue [36], the lipid profile [12,31] and fatal and non-fatal cardiovascular events [38]. In the study by Razvi et al. performed in a real life setting, it was shown (in a real life setting), that LT4 treatment decreased the all-cause mortality rate in individuals <70 years, but not in the group >70 years and that the impact of SCH on the cardiovascular outcome was only significant when TSH levels exceeded 7 mIU/L [14,38,39]. Some authors believe that the absence of the association between SCH and morbidity/mortality in older patients is due to the late onset of SCH and/or misclassification due to a diagnosis based on a single assessment of TSH and the use of TSH reference ranges, that are not age-specific [41,45].

The aims of our study were therefore: 1) to investigate whether the prevalence of thyroid dysfunction and autoimmunity was different between younger and older individuals; 2) to determine age-specific reference ranges and 3) to investigate whether the prevalence of thyroid dysfunction changed when the age-specific reference ranges were used.

2. Subjects and methods

2.1. Overall study design

The CHU St-Pierre is a down town university referral hospital in Brussels (Belgium). In this retrospective study, we started our analyses from laboratory data of 21,333 individuals in who TSH was measured of TSH analysis during the period 01-01-2015 to 31-07-2015. A first selection was made by eliminating subjects in who no TPO-abs were measured ($n = 17.915$). Of the remaining individuals, the medical files were thoroughly investigated and strict exclusion criteria were applied. Reasons for exclusion were: the use of LT4, *anti*-thyroid drugs, patients in the immediate pre- or post-thyroidectomy phase, pregnancy and ovarian hyperstimulation, amiodarone and corticoid use, severe illness (infections) and patients hospitalised at the intensive care unit. Also were individuals <20 years were excluded. Finally, we included the results of serum TSH, FT4 and TPO-abs, that were determined in the same individual at the same day from 676 individuals in the study ($n = 676$). Subsequently, we excluded for the calculation of age-specific reference ranges patients with TAI ($n = 125$), very high ($n = 2$) and low ($n = 2$) serum TSH excluded and data from, to include finally 547 individuals (cf flowchart in Fig. 1). After Log10 transformation of serum TSH levels, the data were normally distributed and age-specific ranges (percentile 2.5 and 97.5) were calculated for both age groups.

Thyroid function tests (TSH and FT4) and thyroid autoimmune parameter (TPO-abs) were expressed as both continuous values and categorical data (besides FT4) in 2 groups of individuals (<60 and ≥60-year-old). According to the commercial assay reference ranges, TAI was present when TPO-abs were >60 kIU/L, SCH when TSH levels >4.0 mIU/L and sch in is case of TSH <0.3 mIU/L.

We were also able to document the presence of nodules or a goiter in 194 patients.

The study was approved by the institutional review board (AK/16-01-16/4611).

2.2. Serum assay

All provisions were implemented by the laboratory of hormonology of our institution. Serum TSH, FT4 and TPO-abs levels were measured using the Chimiluminescence Centaur XP Siemens immunoanalyzer. The reference values were 0.3–4.0 mIU/L, 0.8–2.0 ng/dL and <60 kIU/L for TSH, FT4 and TPO-Abs, respectively. The total imprecision CVs

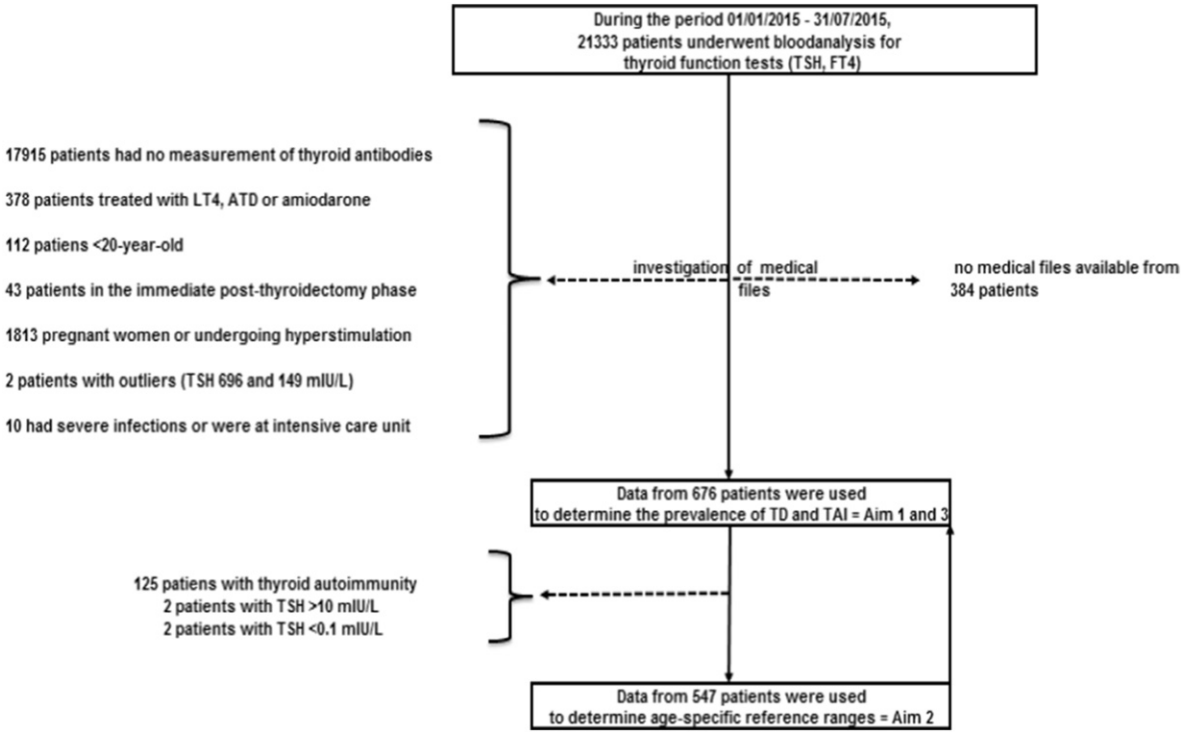

Fig. 1. Flowchart illustrating the selection of the finally included patients in the study.